CLINICAL PROFILE OF LEAN BODY WEIGHT TYPE2 DIABETES -PATIENTS IN COMPARISON WITH OBESE AND NORMAL WEIGHT TYPE 2 DIABETES MELLITUS PATIENTS

DISSERTATION SUBMITTED FOR THE FULFILLMENT OF

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CHENNAI, TAMILNADU.

CERTIFICATE

This is to certify that this dissertation entitled ***"CLINICAL PROFILE OF LEAN BODY WEIGHT TYPE 2 DIABETES MELLITUS PATIENTS IN COMPARISON WITH OBESE AND NORMAL WEIGHT TYPE 2 DIABETES MELLITUS PATIENTS"*** submitted by ***DR. S. SIVAKUMAR*** to the faculty of Medicine, The Tamil Nadu Dr. M.G.R. Medical University, Chennai is in partial fulfillment of the requirement for the award of MD Degree Branch I (General Medicine) is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I, **Dr. S. SIVA KUMAR**, solemnly declare that the dissertation titled **"CLINICAL PROFILE OF LEAN BODY WEIGHT TYPE 2 DIABETES – PATIENTS IN COMPARISON WITH OBESE AND NORMAL WEIGHT TYPE 2 DIABETES MELLITUS PATIENTS"** has been prepared by me.

This is submitted to the Tamil Nadu, Dr. M.G.R. Medical University Chennai, in partial fulfillment of the regulations for the award of MD degree Branch I (General Medicine).

Place : Madurai

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CONTENTS

INTRODUCTION

Diabetes Mellitus is a group of metabolic disorders characterized by, a deficiency of insulin secretion and / or insulin effect, which causes hyperglycemia, disturbances of carbohydrate, fat and protein metabolism and a constellation of chronic complications.

Diabetes is and will remain a threat to global health. World wide diabetes probably affects 150 million people and its prevalence is predicted to double by 2015.

The incidence of diabetes is showing an alarming rise in developing countries, particularly in India. 60-80% of the diabetics in developed countries are obese. Whereas in India we find that clinical profile of diabetics is different.

Most of the patients attending our diabetic clinic are not obese as defined by existing parameters such as BMI. It is interesting to note that most patients fall in normal weight group and some even lean group. Obesity in type 2 diabetes is uncommon in Indian population compared to western population.

So, it is worth studying the clinical profile of lean type 2 diabetes, by comparing with normal and obese population with type 2 diabetes.

REVIEW OF LITERATURE

Diabetes Mellitus comprises a group of metabolic disorders that share the phenotype of hyperglycemia due to absolute or relative deficiency of insulin. Several distinct types of Diabetes Mellitus exist and are caused by a complex interaction of genetics, environmental factors and life style choices. Lack of insulin affects the metabolism of carbohydrates, protein and fat and causes a significant disturbance of water and electrolyte homeostasis. Though acute metabolic decompensation is fatal, long standing metabolic derangement is frequently associated with permanent and preventable functional and structural changes in the cells of the body, with those of the vascular system being particularly susceptible. These changes lead to the development of well defined clinical entities the so called complications of diabetes which characteristically affect the eye, kidney and the nervous system.

Classification

Although all forms of DM are characterised by hyperglycemia the pathogenic mechanisms by which hyperglycemia arises differ widely. Some forms of DM are characterised by an absolute insulin deficiency or a genetic defect leading to defective insulin reaction,

whereas other forms share insulin resistance as their underlying etiology.

The two broad categories are designated as Type 1 and Type 2

Type lA Diabetes Mellitus results from autoimmune beta cell destruction, which usually leads to insulin deficiency. Type 1 B Diabetes Mellitus is also characterised by insulin deficiency as well as tendency to develop ketosis. But individuals with type 1 B Diabetes Mellitus lack immunologic markers indicative of an autoimmune destructive process of beta cells.

Type 2 Diabetes Mellitus is a heterogeneous group of disorders usually characterised by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production.

Other types of Diabetes Mellitus:

Other etiologies of Diabetes Mellitus include specific genetic defects in insulin secretion or action, metabolic abnormalities that impair insulin secretion, and a host of conditions that impair glucose tolerance.

Maturity onset diabetes of the young (MODY) is a subtype of Diabetes Mellitus characterised by autosomal dominant inheritance, early onset of hyperglycemia and impairment in insulin secretion. Mutation is the insulin receptor cause a group of rare disorders characterised by severe insulin resistance.

Diabetes Mellitus can result from pancreatic exocrine disease when the majority of pancreatic islets (>80%) are destroyed. Endocrinopathies such as Acromegaly and Cushing's disease, present with Diabetes Mellitus. Rarely viral infections such as rubella have been implicated in pancreatic islet cell destruction.

Gestational diabetes mellitus:

Insulin resistance related to the metabolic changes of late pregnancy increases insulin requirements and may lead to hyperglycemia or impaired glucose tolerance.

Epidemiology:

Diabetes remains as a threat to global health. World wide the prevalence of Diabetes is estimated to increase from 4% in 1995 to 5.4% by the year 2025. India has the dubious distinction of having the largest number of diabetics in the world.

The prevalence 'of Diabetes in India Study (PODIS) showed that type 2 Diabetes Mellitus was found in 7.06% of the population, which is expected to double by 2015. Diabetes Mellitus is the leading cause of end stage renal disease, non traumatic lower extremity amputation and adult blindness in U.S. The increasing prevalence of Diabetes Mellitus is largely attributed to increasing obesity and reduced activity levels.

The prevalence of Type 2 DM and its harbinger, IGT is highest in certain pacific islands, intermediate in countries such as India and United States, relatively less in Russia and China.

This variability is likely due to genetic, behavioral and environmental factors.

Criteria for the Diagnosis of Diabetes Mellitus

(National Diabetes Data Group and World Health Organisation)

- Symptoms of Diabetes plus random blood glucose concentration $\geq$ 11.1 mmol/L (200 mg/dl)[a]

  (or)

- Fasting plasma glucose $\geq$ 7.0 mmol/L (126 mg/dl)[b]

  (or)

- Two hour plasma glucose $\geq$ 11.1 mmol/L (200 mg/dl) during an oral glucose tolerance test [c]

a) Random is defined as without regard to time since the last meal.

b) Fasting is defined as no caloric intake for at least 8 hours.

c) The test should be performed using a glucose load containing the equivalent of 75 gm anhydrons – glucose dissolved in water : not recommended for routine clinical use.

Source : Modified from American Diabetes Association, 2004

PATHOGENESIS

Type 1 Diabetes Mellitus:

Type 1 A Diabetes Mellitus develops as a result of the synergetic effects of genetic environmental and immunologic factors that ultimately destroy the pancreatic beta cells.

1. Genetic Factors :-

Account for one third of the susceptibility to Type 1 Diabetes, the inheritance of which is polygenic. Over 20 different regions of the

human genome show some linkage with type 1 diabetes, but most interest has focused on the human leucocyte antigen (HLA), on the short arm of chromosome 6. This focus is designated IDDM 1. The HLA haplotypes DR3 and / or DR4 alleles are associated with increased susceptibility to type 1 diabetes.

2. Environmental factors:-

Although genetic susceptibility to be a prerequisite for the development of type 1 diabetes, the concordance rate between monozygotic twins is less than 40%. Environmental factors have an important role in promoting clinical expression of the disease.

"The hygiene hypothesis" :- Lack of exposure to pathogenic organisms in early childhood limits maturation of the immune system and increases susceptibility to autoimmune disease.

3. Viruses :-

Several viruses have been implicated, including mumps, Coxsackie B_4, retroviruses, rubella (in utero) Cytomegalovirus and Epstein – Barr virus.

4. Diet :-

Bovine serum albumin (BSA), a major constituent of cow's milk, has been implicated in triggering type 1 diabetes. It has been shown that children who are given cow's milk early in infancy are more likely to develop type 1 diabetes than who are breast fed.

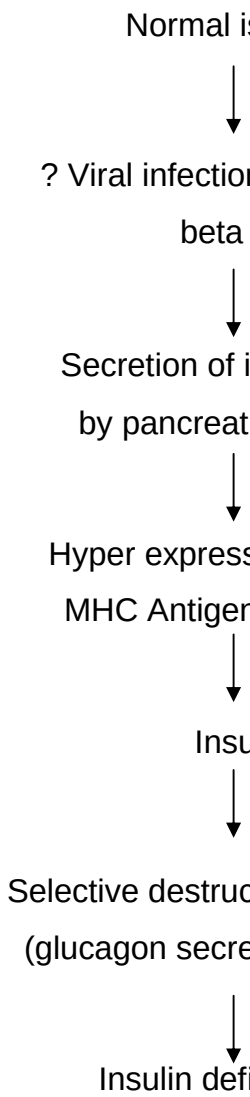
5. Stress :-

Stress may progress the development of type 1 diabetes, by increasing counter regulatory hormones and possibly by modulating immune activity.

6. Immunological factors

Type 2 diabetes is a slow T cell mediated autoimmune disease. Family studies have produced evidence that destruction of the insulin – secreting cells in the pancreatic islets takes place over many years.

Pathogenesis of Type 1 Diabetes



Type 2 Diabetes Mellitus

Type 2 Diabetes mellitus commonly occurs in subjects who are obese and insulin resistant, but these two factors alone are insufficient to cause diabetes unless accompanied by impaired beta cell function.

1. Genetics

Genetic factors are more important in the Aetiology of type 2 DM than type 1 diabetes, as shown by studies in monozygotic twins where concordance rates of type 2 diabetes approach 100%.

2. Environmental Factors

The majority of cases of type 2 diabetes are multifactorial in nature, with interaction of environmental and genetic factors.

a) ***Life style :-*** over eating, especially when combined with obesity and underactivity.

b) ***Malnutrition in utero :-*** It is proposed that, (but not yet proven), malnutrition in utero may programme – beta cell development and metabolic functions at a critical period, so predisposing to type 2 diabetes later in life.

c) ***Age :*** Age is an important risk factor for type 2 diabetes. Type 2 Diabetes principally a disease of the middle aged and elderly, affecting 10% of the population over the age of 65.

d) ***Pregnancy :*** During normal pregnancy, insulin sensitivity is reduced through the action of placental hormones and this affects glucose tolerance.

Pathogenesis of Type 2 Diabetes Mellitus

i) Insulin resistance

ii) Pancreatic Beta cell failure

1. Insulin Resistance

Increased hepatic production of glucose and resistance to the action of insulin in muscle are invariable in both obese and non obese patients with type 2 diabetes. Insulin resistance may be due to

a) an abnormal insulin molecule

b) an excessive amount of circulating antagonists or

c) Target tissue defects

The last is the most common cause of insulin resistance in type 2 diabetes.

2. Pancreatic Beta Cell Failure

In type 2 DM, there is only moderate reduction in the total mass of pancreatic islet tissue which is consistent with a measurable fall in plasma insulin concentration. Some pathological changes are typical of type 2 diabetes, most constituent of which is deposition of amyloid.

While beta cell numbers are reduced by 20-30% in type 2 diabetes, alpha cell mass is unchanged and glucagons secretion is increased, which may constituents to the hyperglycemic.

Some people with type 2 diabetes, most of whom are not overweight, have advanced pancreatic beta cell failure at the time of presentation and require early treatment with insulin.

Complications of DM :

Acute Complications:

Diabetic ketoacidosis (DKA) and Non ketotic hyperosmolar coma (HONK) are acute complications of diabetes. DKA is seen primarily in individuals with type 1 Diabetes Mellitus, and HONK is seen in individuals with type 2 Diabetes Mellitus. Both disorders are associated with absolute or relative insulin deficiency, volume depletion and altered mental status. Both are associated with potentially serious complications if not promptly diagnosed and treated.

Chronic complications:

Chronic complication of DM affect many organ systems and are responsible for majority of morbidity and mortality.

Chronic complications of Diabetes Mellitus:

Microvascular:

Eye disease: Retinopathy

Macular oedema

Cataract

Glaucoma

Neuropathy: Sensory and Motor

Autonomic

Nephropathy:

Macrovascular :

- Coronary artery disease
- Peripheral vascular disease
- Cerebrovascular disease

Others:

- Gastrointestinal
- Genito urinary
- Dermatologic

The risk of complications of both type 1 and type 2 increase as a function of the duration of hyperglycemia. They usually become apparent in the second decade of hyperglycemia.

Mechanism of complications:

Three major theories have been proposed to explain the emergence of complications.

1. Increased intracellular glucose leads to the formation of advanced glycosylation end products (AGE's) via non enzymatic glycosylation of cellular proteins, AGE's have been shown to cross link. Proteins, accelerate atherosclerosis, promote glomerular dysfunction, reduce nitric oxide synthesis, induce endothelial dysfunction and alter the extracellular matrix composition and structure.
2. Hyperglycemia increases glucose metabolism via the sorbitol pathway. Increased intracellular glucose is converted to sorbitol by the enzyme aldose reductase. Increased sorbitol concentrations affect several aspects of cellular physiology and may lead to cellular dysfunction.
3. Hyperglycemia increases the formation of diacylglycerol leading to activation of certain isoforms of protein kinase C, which in turn, affect a variety of cellular events that lead to Diabetes Mellitus related complications.

Finally oxidative stress and free radical generation may also promote the development of complication.

Diabetic Retinopathy:

Diabetic retinopathy is the most common cause of blindness in adults.

Hyperglycemia increases retinal blood flow and metabolism and has direct effects on retinal endothelial cells and pericytes, loss of which impairs vascular auto regulation. The resulting uncontrolled blood flow increases production of vasoactive substances and endothelial cell proliferation resulting in capillary closure. This causes chronic retinal hypoxia and stimulates production of growth factors, including vascular endothelial growth factor (VEGF) to stimulate endothelial cell growth (causing new vessel formation) and increased vascular permeability (causing exudative damage).

Diabetic Nephropathy:

Diabetic Nephropathy is the leading cause of end stage renal disease (ESRD) in many countries.

Mechanism of chronic hyperglycemia to ESRD involve

1. interaction of soluble factors (AT II, AGEs, Endothelin)
2. hemodynamic alterations in renal microcirculation.
3. structural charges in glomerulus.

Diabetic neuropathy

"A descriptive term meaning a demonstrable disorder, either clinically evident or subclinical, that occurs in the setting of diabetes mellitus without other causes for peripheral neuropathy. The neuropathic disorder includes manifestations in the somatic and/or autonomic parts of the peripheral nervous system.

Aetiopathogenesis of Diabetic Neuropathy

Hypotheses concerning the multiple etiologies of diabetic neuropathy include a metabolic insult to nerve fibers, neurovascular insufficiency, autoimmune damage, and neurohormonal growth factor deficiency. Several different factors have been implicated in this pathogenic process. Hyperglycemic activation of the polyol pathway leading to accumulation of sorbitol and potential changes in the NAD:NADH ratio may cause direct neuronal damage and/or decreased nerve blood flow.(Greene et al,1983) Activation of protein kinase C induces vasoconstriction and reduces neuronal blood flow(Veves et al,200 1) Increased oxidative stress, with increased free radical production, causes" vascular endothelium damage and reduces nitric oxide bioavailability (Cameron et ai, 1997)Alternately, excess nitric oxide production may result in formation of peroxynitrite and damage endothelium and neurons, a process referred to as nitrosative

stress. In a subpopulation of individuals with neuropathy, immune mechanisms may also be involved. Reduction in neurotrophic growth factors, deficiency of essential fatty acids, and formation of advanced glycosylation end products (localized in endoneurial blood vessels (Brownlee ,1992) also result in reduced endoneurial blood flow and nerve hypoxia with altered nerve function. The result of this multifactorial process may be activation of polyADP ribosylation depletion of A TP, resulting in cell necrosis and activation of genes involved in neuronal damage".

Diabetic autonomic neuropathy

A subtype of the peripheral polyneuropathies that accompany diabetes, Diabetic autonomic neuropathy can involve the entire autonomic nervous system (ANS). ANS vasomotor, visceromotor, and sensory fibers innervate every organ. Diabetic autonomic neuropathy may be either clinically evident or subclinical. It is manifested by dysfunction of one or more organ systems (e.g., cardiovascular, gastrointestinal [GI], genitourinary, sudomotor, or ocular). Indeed, because the vagus nerve (the longest of the ANS nerves) accounts for roughly 75% of all parasympathetic activity), and Diabetic autonomic neuropathy manifests first in longer nerves. Symptoms suggestive of autonomic dysfunction may be common they may frequently be due to other causes rather than to true autonomic neuropathy. Subclinical

autonomic dysfunction can, however, occur within a year of diagnosis in type 2 diabetes patients (Pfeifer et al,1984).Because of its association with a variety of adverse outcomes including cardiovascular deaths, cardiovascular autonomic neuropathy (CAN) is the most clinically important and well-studied form of Diabetic autonomic neuropathy.

Macrovascular Complications

1. Cardiovascular Morbidity and Mortality

Framingham Heart study revealed a marked increase in congestive heart failure, coronary artery disease, myocardial infarction (MI), Peripheral arterial disease and sudden death (risk increase from one to five fold) in DM.

American Heart Association recently designated Diabetes mellitus as a major risk factor for cardiovascular disease (same category as smoking, hypertension and hyperlipedemia).

The absence of chest pain (silent ischemic) is common in individuals with diabetes and a thorough cardiac evaluation is indicated. Coronary artery disease is more likely to involve multiple vessels in individuals with diabetes mellitus.

2. Hypertension

Hypertension in diabetes mellitus can accelerate other complications of DM, particularly cardiovascular disease, and nephropathy. Blood pressure goal in individual with diabetes is < 130 / 80 mm Hg. Hypertension is often difficult to control with a single agent especially in type 2 diabetes, multiple antihypertensive agents are usually required.

3. Dyslipidemia

Individuals with diabetes may have several forms of dyslipidemia. Because of additive – cardiovascular risk of hyperglycemia and hyperlipidemia, lipid abnormalities should be aggressively detected and treated. Most common pattern of dyslipidemia is hypertriglyceridemia and reduced HDL cholesterol levels.

Target lipid values in diabetic individual without cardiovascular disease should be,

- LDL < 100 mg/dl
- In men, HDL (>40 mg/dl)

  In women, HDL (>50 mg/dl)
- Triglycerides < 150 ml/dl

4) Lower extremity complications

Diabetes is the leading cause of non traumatic lower extremity amputation in U.S. Foot ulcers and infections are also a major source of morbidity in individuals with DM.

5) Infections

Individuals with DM have a greater frequency and severity of infection. The reasons for this include incompletely defined abnormalities in cell mediated immunity and phagotypic function associated with hyperglycemia, as well as diminished vascularisation.

Cardiac and other fungal infections, emphysematons infections of the gall bladder and urinary tract, pneumonia and skin and soft tissue infections are all more common in diabetic population. However gram negative organisms, in tuberculosis and S. Aureus also more frequent pathogens.

Diabetic skin complications

Some of them are

1. **Diabetic dermopathy** – begins as a erythematous area and evolves into an area of circular hyper pigmentation.
2. **Necrobiosis Lipoidica – Diabeticorum –** usually begins in the pretibial region as an erythematous plaque or papules

that gradually enlarge, darken and develop irregular – margins with atrophic centers and central ulceration.

3. **Acanthosis nigricans** – Hyperpigmented velvety plaques seen on the neck, axilla, or extensor surfaces, is sometimes a feature of severe insulin resistance.
4. **Granuloma Annulare** – erythematous plaques on the extremities or trunk.
5. **Scleredema** – Area of skin thickening on the back or neck at the site of previous superficial infections.
6. **Lipoatrophy and Lipohypertrophy**
7. **Xerosis** and **pruritus** are common.

Clinical profile of lean type 2 diabetes

Articles review

1. Clinical profile of lean type 2 diabetes – study conducted at Madras Diabetes Research Foundation, India with 347 lean, 6274 normal and 3252 obese type 2 diabetes patients in 2002 observed.
    a. 60% are non obese and lean type 2 DM constituted 3.5%.
    b. Increased prevalence of retinopathy, nephropathy and neuropathy in lean type 2 DM patients.

2. Clinical profile of type 2 diabetes mellitus and body mass index – is there any correlation?. Study conducted with 500 patients at Manipal, Kasthuriba Medical College by Prabhu Mukhyaprana M, in 2004, observed,
    a. Majority (65%) belonged to normal weight diabetes group, and 7.1% were lean diabetics.
    b. Most of the lean diabetics were males (65%) with less positive family history.
    c. There was 2 linear increase in number of patients having abnormal WHR with increase in BMI.
    d. Microvascular complications were found in similar, proportion in all groups.
    e. Lean diabetics are less prone to develop macro vascular complications like HT and IHD.
    f. Lean diabetics have more severe hyperglycemia and poor metabolic control.
    g. Analysis of lipid profile showed, all the parameters were lower in lean diabetics compared to all other groups i.e. normal and obese patients.

3. Clinical profile of lean body weight type 2 DM patients in comparison with obese and non obese type 2 diabetes patients.

Study conducted at Jamnagar, M.P. Shah Medical College by Gohel DR, Deszi VK, in 2002-2003 observed very similar results as previous studies. In addition,

i) Increased incidence of higher fasting plasma glucose (239±42.5) in lean diabetics.
ii) Peripheral neuropathy (52%) and infections (42%) were the commonest presenting clinical features in lean patients.

4. Increased prevalence of Retinopathy, nephropathy and neuropathy in lean diabetics; Mohan et al .

5. Studies by Banerji et al and Dass et al had showed slight increase in Triglycerides (TGL) and HDL in lean diabetes.

6. Japanese study by Ikeda et al showed no major differences in lipid profile in lean diabetics irrespective of glycemic status.

AIM OF THE STUDY

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1. To Study and compare the clinical profile of Lean Body weight Type 2 Diabetes Mellitus patients – in comparison with obese and Normal weight Type 2 DM patients, by age, sex, family history and Anthropometry.

2. To compare the "presenting complications" of the lean with normal weight and obese type 2 Diabetes patients.

3. To compare the Biochemistry profile of the lean type 2 Diabetes with normal and obese type 2 DM, that is Blood Glucose, Urea, Serum Creatinine and Lipid profile.

MATERIALS AND METHODS

MATERIALS AND METHODS

Materials

The study included hundred patients with Type 2 Diabetes mellitus attending the out patients in Departments of Medicine and Diabetology, Government Rajaji Hospital between July 2005 and June 2006, one year period.

Those hundred patients divided into three groups based on Body Mass Index (BMI).

- ★ **Group A:** BMI < 18.5 Kg/m^2 (Lean Body Weight Type 2 DM)
- ★ **Group B:** BMI, between 18.5 and 25 Kg/m^2 (Normal Weight Type 2 DM).
- ★ **Group C:** BMI > 25 Kg/m^2 (Obese Type 2 DM)

A careful detailed history were taken from each person, i.e. Age of onset, duration, any positive family history, dietary pattern, presenting complaints – at the time of diagnosis etc.

Detailed examination were done for all the hundred patients to find out various complications, if any.

Biochemically, Blood glucose (Both fasting and post prandial), Blood urea, Serum Creatinine, Lipid profile were analysed in all the three groups.

Selection of cases

Cases included in the study were selected as per the records available with them.

Duration of disease, Body Mass Index, Waist Hip Ratio, current Blood Glucose, Urea, Serum Creatinine and Lipid profile were taken into consideration.

Exclusion Criteria for cases

1. Presence of pulmonary tuberculosis history.
2. Presence of other chronic illnesses that could affect Body weight like chronic liver and chronic kidney disease.
3. Type 2 Diabetes patients with Age of onset less than 30 years.

4. History wise, particularly in lean patients those who were normal or obese at the time of presentation, now lost the body weight significantly after type 2 Diabetes mellitus detection.
5. Patient with history of Cancer, Cachexia and HIV.

Selection of Controls

Control cases were normal weight as well as obese patients with Type 2 Diabetes Mellitus.

Methods

1. Height (in meter), Weight (in kg) measured in all patients. BMI (Body Mass Index) calculated based on the formula,

$$\text{BMI (Kg/m}^2\text{) (Quetelet)} = \frac{\text{Weight (kg)}}{\text{Height (in m}^2\text{)}}$$

2. Waist hip Ratio (W/H Ratio) 'Waist Circumference' measured at midpoint between the costal margin and anterior superior iliac spine.

   Hip Measurement taken as maximum diameter at the greater trochanter.

Waist / Hip Ratio (WHR) was calculated in each case.

Waist Hip ratio was considered abnormal if > 0.95 for males and > 0.8 for females.

3. Skin Fold Thickness (SFT)

Skin Fold Thickness was measured at standard sits such as the Biceps, Triceps, infrascapular, and supra iliac region using a Harpenden Calliper or similar device.

The Calliper is designed so that the jaws of the device remain parallel and constant pressure is exerted between them or different skin fold thicknesses.

Triceps skinfold, midway between abdomen and olecranum, is used in our study.

Patients were clinically screened for microvascular and macrovascular complications.

- ★ Patients were considered as hypertensive if blood pressure was > 130/85 mm Hg.

- ★ Patients were considered as having ischemic heart disease based on ischemic changes in the ECG or by demonstrating hypokinetic or akinetic segment in the echocardiogram for selected patients.

- ★ Ophtholmoscopy was done to diagnose diabetic retinopathy.

- ★ Neuropathy was diagnosed, based on subjective symptoms or objective evidence in the form of loss of ankle jerk or glove and stocking type of anaesthesia.

- ★ Nephropathy was diagnosed based on blood urea and serum creatinine values.

- ★ Fasting, post prandial glucose, fasting lipid profile and other relevant investigations were done in each case.

Definitions and Cut Off values for the study

1. **Body Mass Index (BMI)**

   18.5-24 (kg/m^2) – taken as normal value

   < 18.5 (kg/m^2) – lean body weight

   > 25 (kg/m^2) – obese body weight

2. **Waist Hip Ratio**

WHR - > 0.8 – is taken as abnormal value in female.

> 0.95 in male as abnormal value.

3. **SFT (Skin Fold Thickness)**

(in mm)

> 12.5 – abnormal in male.

> 16.5 – abnormal in females.

4. **Fasting 'Hyper glycemia' – (FBS)**

'Fasting' means 8 hours fasting overnight.

Fasting Hyperglycemia means if Blood glucose value > 126 mg%

5. **Post prandial Hyperglycemia (PPBS)**

Post prandial measures at 2 hours after the meals.

Post prandial hyperglycemia means if value > 200 mg%

6. **Lipid Profile**

Lipid profile taken after 8 hours overnight fasting.

Normal Value	Range
Free cholesterol	150-200 mg
Triglycerides	75-150 mg%
HDL	30-60 mg%
VLDL	20-40 mg%
LDL	80-150 mg%

Others

Blood is drawn from each patient under recommended ideal conditions to determine the fasting and post prandial Blood sugar, urea, serum creatinine and Lipid profile.

Ethical Committee Approval

The present study was approved by the ethical committee.

Statistical Analysis

Statistical Analysis of data was done by using the software – Epidemiological Information Package (EPI 6) developed by World Health Organisation.

Frequencies, Percentages, Range, Median, Mean, S.D. and 'p' values were calculated using this package.

RESULTS AND OBSERVATIONS

RESULTS AND OBSERVATIONS

Table 1

Characteristics of the study population

Characteristics	Range	Median	Mean	S.D.
Age	30-90	50	49.8	12.3
BMI	16-31	22.25	22.89	4.25
W/H Ratio				
a) Males	0.78-1.04	0.9	0.91	0.05
b) Females	0.74-1.02	0.86	0.87	0.07
c) Total	0.74-1.04	0.9	0.9	0.06
SF Thickness				
a) Males	8-18	12	12.2	2.4
b) Females	8-22	11.5	12.5	3.7
c) Total	8-22	12	12.3	3.0
Fasting Blood Sugar	60-445	215	221.3	86.4
P.P. Blood Sugar	130-642	280	306.3	111.9
Free cholesterol	110-381	204	213.9	60.0
TGL	95-327	160	158.2	34
LDL	36-317	104	121.2	60.4
HDL	25-45	40	37.3	5.0
VLDL	19-65	32	32.1	7.9
Systolic BP	100-220	130	132.4	23.1
Diastolic BP	60-120	80	85.3	11.8

Table 2

Characteristics	No.	%
Sex		
a) Males	56	56
b) Females	44	44
Family History		
a) Yes	24	24
b) No	76	76
Complications		
a) Cardiac		
Yes	16	18
No	82	82
b) Renal		
Yes	50	50
No	50	50
c) Neuro		
Yes	44	44
No	56	56
d) Retinopathy		
Yes	38	38
No	62	62
e) Infections		
Yes	36	36
No	64	64
f) HT		
Yes	30	30
No	70	70
BMI		
a) Lean	18	18
b) Normal	52	52
c) Obese	30	30

RELATIONSHIP BETWEEN BODY MASS INDEX AND OTHER PARAMETERS

Table 3

Age and BMI

Age Group	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
< 40	4	22.2	20	38.5	6	20
41-50	4	22.2	20	23.1	8	26.7
51-60	6	33.4	12	23.1	16	53.3
>60	4	22.2	8	15.3	-	-
Total	18	100	52	100	30	100
Mean	53.2		48.1		50.7	
S.D.	17.9		11.7		9.6	
P	0.4695					

There is no statistically significant relationship between age and BMI.

Table 4

Sex and BMI

Sex	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Male (56)	8	14.3	38	67.9	10	17.9
Female (44)	10	22.7	14	31.8	20	45.5
P	0.0364					

There is statistically significant relationship between sex and BMI.

Table 5

Family History and BMI

Family History	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Yes (42)	2	4.8	26	61.9	14	33.3
No(58)	16	27.6	26	44.8	16	27.6
P	0.0399 (Significant)					

Percentage of lean cases is low in persons with family history.

Table 6

Waist Hip Ratio and BMI

W/H Ratio	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Normal (54)	12	22.2	38	70.4	4	7.4
Abnormal (46)	6	13	14	30.4	26	56.5
Mean W/H Ratio	0.85		0.9		0.92	
S.D.	0.06		0.06		0.06	
P	0.0379					

Waist Hip Ratio has a statistically significant relationship with BMI.

Table 7

S.F Thickness and BMI

S.F Thickness	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Normal (78)	16	20.5	40	51.3	22	28.2
Abnormal (22)	2	9.1	12	54.5	8	36.4
Mean SF	10		12.25		13.9	
S.D.	2.06		2.74		3.11	
P	0.0016					

Statistically significant relationship exists between SF Thickness and BMI. As BMI increases, mean SF Thickness also increases.

Table 8

Fasting Blood Sugar and BMI

Fasting Blood Sugar	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Normal (14)	2	14.2	6	42.9	6	42.9
Abnormal(86)	16	18.6	46	53.5	24	27.9
Mean	270.6		202.3		172.6	
S.D.	105.9		76.6		55.6	
P	0.0425 (Significant)					

Lean persons have higher fasting blood sugar levels than obese persons. The difference is also statistically significant.

Table 9

Post Prandial Blood Sugar and BMI

Post prandial Blood Sugar	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Normal (8)	2	25	4	50	2	25
Abnormal (92)	16	17.4	48	52.2	28	30.4
Mean	305.6		317.5		287.5	
S.D.	121.7		130.4		66.7	
p	0.9664					

No significant relationship

Table 10

Free Cholesterol and BMI

Free Cholesterol	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Normal (48)	14	29.2	24	50	10	20.8
Abnormal (52)	4	7.7	28	53.8	20	38.5
Mean	180.1		215.9		230.7	
S.D.	53.3		61.9		55.7	
p	0.0765					

As BMI increases, free cholesterol levels also increase. But the difference is not statistically significant.

Table 11

TGL and BMI

TGL	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Normal (40)	12	30	20	50	8	20
Abnormal (60)	6	10	32	53.3	22	36.7
Mean	145.4		158.8		164.6	
S.D.	20.2		41.3		24.9	
p	0.117					

No significant relationship.

Table 12

LDL and BMI

LDL	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Normal (76)	14	18.4	42	55.3	20	26.3
Abnormal (24)	4	16.7	10	41.7	10	41.7
Mean	101.4		116.6		140.9	
S.D.	43.5		62.2		63.9	
p	0.0849					

Not significant.

Table 13

HDL and BMI

HDL	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Normal (92)	18	19.6	50	54.3	24	26.1
Abnormal (8)	-	-	2	25	6	75
Mean	41		38.2		33.7	
S.D.	2		3.6		6.2	
p	0.0037					

As BMI increases, HDL levels decrease. The relationship is statistically significant.

Table 14

VLDL and BMI

VLDL	BMI					
	Lean		Normal		Obese	
	No.	%	No.	%	No.	%
Normal (94)	18	19.1	50	53.2	26	27.7
Abnormal (6)	-	-	2	33.3	4	66.7
Mean	29		31.65		34.87	
S.D.	3.94		8.2		8.53	
p	0.0618					

Not significant.

Table 15

Complications and BMI

Cardiac, Renal, HT Incidence and BMI

BMI	Complications											
	Cardiac				Renal				H.T.			
	Present		Absent		Present		Absent		Present		Absent	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Lean (18)	-	-	18	100	10	55.6	8	44.4	4	22.2	14	77.8
Normal (52)	12	23.1	40	76.9	26	50	26	50	12	23.1	40	76.9
Obese (30)	6	20	24	80	14	46.7	16	53.3	14	46.7	16	53.3
P	0.5491 (Not significant)				0.76 (Not significant)				0.0906 (Not significant)			

B. Neuropathy, Retinopathy and Infections incidence and BMI

BMI	Complications											
	Neuropathy				Retinopathy				Infections			
	Present		Absent		Present		Absent		Present		Absent	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Lean (18)	14	77.8	4	22.2	12	66.7	6	33.3	12	66.7	6	33.3
Normal (52)	24	46.2	28	53.8	14	26.9	38	73.1	12	23.1	40	76.9
Obese (30)	8	26.7	22	73.3	10	33.3	20	66.7	10	33.3	20	66.7
P	0.0399 (Significant)				0.0436 (Significant)				0.0314 (Significant)			

Incidence of neuropathy, Retinopathy and Infection is more in lean patients (77.8%, 66.7% and 66.7% respectively) than in the normal and obese patients. This relationship is statistically significant.

DISCUSSION AND ANALYSIS OF RESULTS

DISCUSSION AND ANALYSIS OF RESULTS

"Diabetes Mellitus" is an age old affliction of man and is the most common metabolic disorder all over the world. The incidence of Diabetes showing alarming rise in developing countries, particularly in India.

Most of the diabetics in developed countries are obese. However in India we have a significant number of diabetics who are either normal weight or even under weight.

Eventhough obesity is considered as part of syndrome X in pathogenesis of type 2 diabetes, in our study, out of 100 patients only 30 patients were obese.

Our study included hundred patients. Among **100 patients**, 56 are males and 44 are females. In our study majority of patients, that is 52 patients (52%) belong to normal weight, 30 patients (30%) belong to obese and **18 patients (18%)** belong to **lean body weight**.

1. Age

In our study, we found there is no particular age group for lean diabetics. But 33.4% of lean diabetics belong to 51-60 years of age, 38.5% of normal weight patients between 30 and 40 years, and 53.3% of obese patients belong to 51-60 years of age group.

2. Sex

There is statistically significant relationship exist in our study between sex and BMI. Slightly higher incidence of female in lean body weight (M : F Ratio = 0.8 : 1). In obese M : F Ratio is 1 : 2 and in normal body weight it is male preponderance (67.9%).

3. Family History

Family history of diabetes is present only in 4.8% of lean diabetics, in comparison it is 61.9% in normal and 33.3% in obese diabetics. So there is less incidence of family history present among lean diabetics.

4. Waist Hip Ratio and BMI

There is a linear increase in number of patients having abnormal Waist Hip ratio with increase in BMI.

Among 100 patients studied, 46 patients having abnormal Waist Hip ratio. Among that it is 13% in lean, 31% in normal and 56% in obese type 2 diabetes having abnormal value.

Eventhough 18% (18) of diabetics patients are lean based on BMI, 6 among them having abnormal Waist hip ratio. So, **Waist hip ratio is a better indicator than BMI** for assessment of obesity .

Skin fold thickness also increases as the BMI increases.

5. Complications

Microvascular complications

Among the microvascular complications **neuropathy (77.8%), Retinopathy (66.7%)** are common in **lean diabetics** in our study which are statistically significant. Only 44.4% of lean diabetics had nephropathy, which is not statistically significant.

In normal weight group, incidence of neuropathy, retinopathy and nephropathy are 46.2%, 26.9% and 50% respectively.

In obese patients, incidence of neuropathy, retinopathy and nephropathy are 26.7%, 33.3% and 46.7%.

Macrovascular Complications

Lean diabetics are **less prone** to develop **macrovascular** complications – like hypertension and Ischemic Heart Disease.

Incidence of hypertension is 22.2% in lean patients as compared to 23.1% in normal and 46.7% in obese diabetics, like wise Ischemic Heart Disease incidence in our study is 0% in lean diabetics as compared to 23.1% in normal and 20% in obese diabetics.

Infections

In our study, 66.7% of lean patients with type 2 diabetes presented with infections as compare to 23.1% in normal and 33.1% in obese patients. Values are statistically significant p value = 0.0314. Majority of the **lean diabetics** in our study group presented with **infections**.

Glycemic Control

Lean diabetics have more severe hyperglycemia with poor metabolic control. Lean persons have **higher fasting blood sugar** (270±105.9) levels than obese and normal weight type 2 diabetes patients. Similarly post prandial – value also high in lean type 2 DM patients. This has been explained by probable **low beta cell reserve**

among lean diabetics. So, Lean diabetics are **insulinopenic** and **highly insulin sensitive**.

Lipid Profile

Regarding lipid profile of lean type 2 diabetes patients, all the parameters are **lower** in lean diabetics compared to all other groups. Moreover, lean diabetics have slightly higher HDL value (41.0±2.0) as compare to normal (38±4) and obese (33±6) diabetics, which is statistically significant.

Also free cholesterol value in lean diabetics are (180 ± 53) as compared to (215.9 ± 61.9) and (230.7 ± 55.7) in obese patients.

Triglycerides value in lean diabetics (145 ± 20) as compared to (158.8 ± 41.3) in normal and (164.6 ± 24.9) in obese diabetics.

So, lean diabetics have **favorable lipid profile** as compared to normal and obese diabetics.

Our study has **limitations**, as it was hospital based in the tertiary – care setting. Incidence of complications might be higher compared to general population or primary case setting. We did not do

insulin level assay, C peptide levels and GAD Antibodies in our lean diabetics due to financial constraints.

In conclusion, type 2 diabetics patients need not always obese. Majority (52%) belongs to normal weight and significant number (18%) of patients even lean in our study. Thus, lean body type 2 DM patients appear to be a distinct variety and a great deal of emphasis is to be given on its clinical profile and natural history.

COMPARATIVE ANALYSIS

COMPARATIVE ANALYSIS

Our study includes 100 patients with type 2 diabetes. Among them normal weight (52%), obese patients (30%) and lean type 2 diabetics (18%). But the study

i) Conducted at Manipal by Prabhu Mukhyaprana in Sudha Vidyasagar included 500 type 2 diabetic patients between July 2000 and January 2001.

ii) The study conducted by Gohul Dr. Desai VK at M.P. Shah Medical College, Jamnagar, published in JAPI, Dec 2003 included 75 patients with Type 2 Diabetes Mellitus.

1. Percentage of Lean Body Weight Type 2 DM Population

In our study, Lean Type 2 DM observed were 18%, as compare to 52% of normal and 30% of obese patients.

- Study conducted (by Mukhyaprana et al) were 7.4% and majority (65%) were normal weight.
- Incidence of lean body weight – Diabetes in various Indian studies ranges from 1.6% as in Ramachandran et al. study to as high as 28% as in Tripathi et al.
- Mohan et al reported an incidence of 3.5%.

2. Age Group

In our study there is no statistically significant relationship between age and BMI observed. 33.6% of lean type 2 DM, were between 51-60 years of age.

i) But study conducted by Prabhu et al, mean age of onset of diabetes in lean were 60.34 ± 13.5 years.

ii) In Gohel DR. et al study it was between 30-40 years.

3. Sex

In our study, lean type 2 Diabetes patients were slightly higher in female sex (22.7%) with sex ratio of 0.8 : 1 – male : female values were statistically significant with 'p' value 0.0364.

i) Study conducted by Prabhu Mukhyaprana M et al observed most lean type 2 DM were males (65% of total lean) type 2 DM which was statistically not significant.

ii) Study conducted by Gohel Dr., Desai VK et al observed male : females ratio - 3 : 2 in lean diabetics.

4. Family History

Positive family history was present only in 4.8% of patients with lean body weight type 2 DM as compare to 61.9% in normal weight and 33.3% of obese patients with type 2 DM which were statistically significant with 'p' 0.0399.

i) Study conducted by Prabhu Mukhyaprana et al observed positive family history in 45% of lean and 62.6% in normal body weight diabetics, results were similar to studies by – Banerji et al and Kannan et al studies.

ii) Study conducted by Gohel DR et al observed low incidence of positive family history (20%) in lean as compared to 40% in normal and 44% in obese patients.

5. BMI and WHR – Are they related?

In our study 13% of lean diabetes had abnormal Waist Hip Ratio as compared to 30.4% in normal and 56.5% in obese patients.

Waist Hip Ratio had a statistically significant ('p' – 0.0379) relationship with BMI.

Previous study conducted at Manipal observed lean diabetics (48%) had abnormal Waist Hip Ratio, stating that significant number of lean diabetics (48%) had abnormal Waist Hip Ratio. This Waist Hip Ratio may thus be a more sensitive indicator of obesity in Indians.

6. Skin fold thickness and Body Mass Index

Statistically significant relationship exists between SF Thickness and BMI.

That is As BMI increases, mean SF thickness also increases.

7. Glycemic Status

In our study, Lean persons have higher fasting blood sugar (270 ± 105.9) levels than obese patients with Type 2 Diabetes, which was statistically significant (p = 0.0425) as compare to normal obese patients with Type 2 Diabetes.

i) Results were similar to studies done by Kannan et al and Italian Study by Pointoroly et al. This has been explained based on low – beta cell reserve in these patients.

ii) Similar results were also observed in study conducted by Prabhu Mukyaprana et al. Fasting blood sugar was 177.08±105.1.

iii) Postprandial blood sugar value in Lean type 2 DM patients were 305.6 ± 121.7 higher, even though statistically not significant.

8. Lipid Profile

Analysis of lipid profile in our study showed interesting results.

★ Type 2 lean diabetics, had lower incidence of dyslipidemia as compared to all other groups. Even though only HDL relationship with BMI were statistically significant.

- ★ In our study HDL values were slightly higher in lean diabetics i.e. (41.0 ± 2.0) as compare to (38 ± 4) in normal and (33 ± 6) in obese patients, which was statistically significant (p – 0.0037).
- ★ Also free cholesterol value in lean diabetics were (180 ± 53) as compared to (215.9 ± 61.9) and (230.7 ± 55.7) in obese patients.
- ★ Triglycerides value in lean diabetics (145 ± 20) as compared to (158.8 ± 41.3) in normal and (164.6 ± 24.9) in obese diabetics.

Previous studies by Banerji et al and Das et al had showed slight increase in TGL and HDL in lean diabetics.

Japanese study by Ikeda et al showed no major differences in lipid profile in lean diabetics, irrespective of glycemic status.

9. Complications

In our study, increased incidence of **microvascular** complications like neuropathy, retinopathy observed which is statistically significant.

77.8% of lean patients, had neuropathy as a presenting complaint as compared to 46.2% in normal and 26.7% in obese patients with a 'p' value of 0.0399 (significant).

Retinopathy also increased in lean type 2 Diabetics with 66.7% in lean, 26.9% in normal and 33.3% in obese patients with a ‘p’ value of 0.0436 (Significant).

In our study nephropathy observed only in 44.4% of lean patients as compared to 50% in normal and 53.3% of obese type 2 diabetics, which is not statistically significant.

Study conducted at Manipal showed microvascular complications were similar in all the 3 groups.

Macrovascular complications like HT, IHD were less in lean diabetics as compared to other groups.

In our study, the incidence of hypertension was 22.2% in lean as compared to 23.1 in Normal and 46.7 % in Obese. Incidence of IHD in lean was 0 % in comparison with 23.1% in normal and 20% in Obese.

Incidence of hypertension was 8.9% and IHD 10.2% IN Nigan et al study.

In Manipal study the incidence of IHD only 2.7% among lean and HT only 16.7% of lean diabetics.

Infections

In our study 66.7% of lean patients with type 2 diabetes presented with infections as compared to 23.1% in normal and 33.3% in obese patients.

Values were specifically significant also. (‘p’ value = 0.0314)

Mohan et al reported increased prevalence of retinopathy, neuropathy and nephropathy in lean diabetics.

Peripheral neuropathy was the commonest presenting complication among lean diabetics in a study by Das et al.

Peripheral neuropathy and **infections** were the commonest presenting clinical features in lean diabetics observed in study conducted by Gohel et al.

SUMMARY

SUMMARY

- ★ Total Number of patients studied – 100. Out of 100 patients, 56 were male and remaining 44 were female.
- ★ Number of lean type 2 DM Patients were 18. Among them 44% were Male and 56% were Female.
- ★ Number of normal weight type 2 diabetics were 52. Among them 73% were male and 27% were female.
- ★ Number of obese type 2 diabetics patients were 30. Among them 33% were male and 67% were female.
- ★ Most of diabetics in our population (52%) have normal body weight. Lean Type 2 Diabetics form significant number (18%).
- ★ Low incidence of positive family history in lean type 2 diabetics (4.8%). Increased incidence of higher fasting plasma glucose in lean diabetics.
- ★ Peripheral neuropathy (77.8%), Retinopathy (66.7%) and infections (66.7%) were the major presenting clinical complications in lean diabetics.
- ★ Most risk factors of atherosclerosis and CAD are less prevalent in lean type 2 diabetes (Normal HDL, and total cholesterol on lower side).

CONCLUSION

CONCLUSION

a. Majority of type 2 diabetes patients in our population having **normal weight (52%)** and **lean body weight contributes to 18%.**

b. Lean diabetics have **more severe hyperglycemia** and poor metabolic control. They are more prone for **microvascular complications** like neuropathy and retinopathy.

c. **Early treatment** with **insulin** in lean type 2 diabetics is mandatory to achieve **good glycemic control** and to prevent future complications.

APPENDIX

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BIBLIOGRAPHY

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PROFORMA

PROFORMA

CLINICAL PROFILE OF LEAN BODY WEIGHT TYPE 2 DM PATIENTS IN COMPARISON WITH OBESE AND NON-OBESE TYPE 2 DM PATIENTS

Date of Registration

Name Age

Address Sex M

Religion F

Special study No.

Single

Married

Occupation

Sedentary

Active

Income

New case **Already treated case** **How long**

PRESENTING SYMPTOMS AT THE TIME OF DETECTION

Symptoms	YES	NO
Polyuria		
Nocturia		
Polydypsia		
Polyphaqia		
Tiredness		
Weight loss		
Giddiness		
Blurrinq of vision		
Skin infection		
Itching		
Vomiting		
Abdominal pain		
Constipation		

Nocturnal Diarrhoea Numbness Pruritus vulvae Sexual Dysfunction Balanitis joint / body pain Ulcer		

Previous treatment Insulin Regular
Tablets
Diet Irregular
Alternative

Previous illness M.I Accidents
HT Operations
PT Other op
Jaundice

Family History of Diabetes Yes/no

Father	Brother	Sons
Mother	Sister	Daughters
Wife	Husband	

Personal History

Fondness for sweets	Yes/no	
Smoking	Yes/no	How long
Alcohol	Yes/no	How long
Vegetarian	Yes/no	
Non- veg	Yes/no	
Total Calories per day		

Examination

General

Acanthosis Nigricans

Skin tag

Xanthoma Xanthelasma
Thyroid swelling

BP Lying
Pulse Standing

Anthropometry

Height Weight Ideal wt.
In cms kgs over wt.
Under wt.
(Lean)

BMI

Waist Hip Waist / hip (WHR)
Circumference circumference
Skin fold thickness

System

CVS
Respiratory
Abdomen
CNS

Opthalmological

INVESTIGATIONS

Urine - Albumin
Sugar
Deposits

Blood sugar Fasting
Post prandial

Blood urea
Sr. creatinine
Lipid profile TCL
LDL
HDL
VLDL
TGL

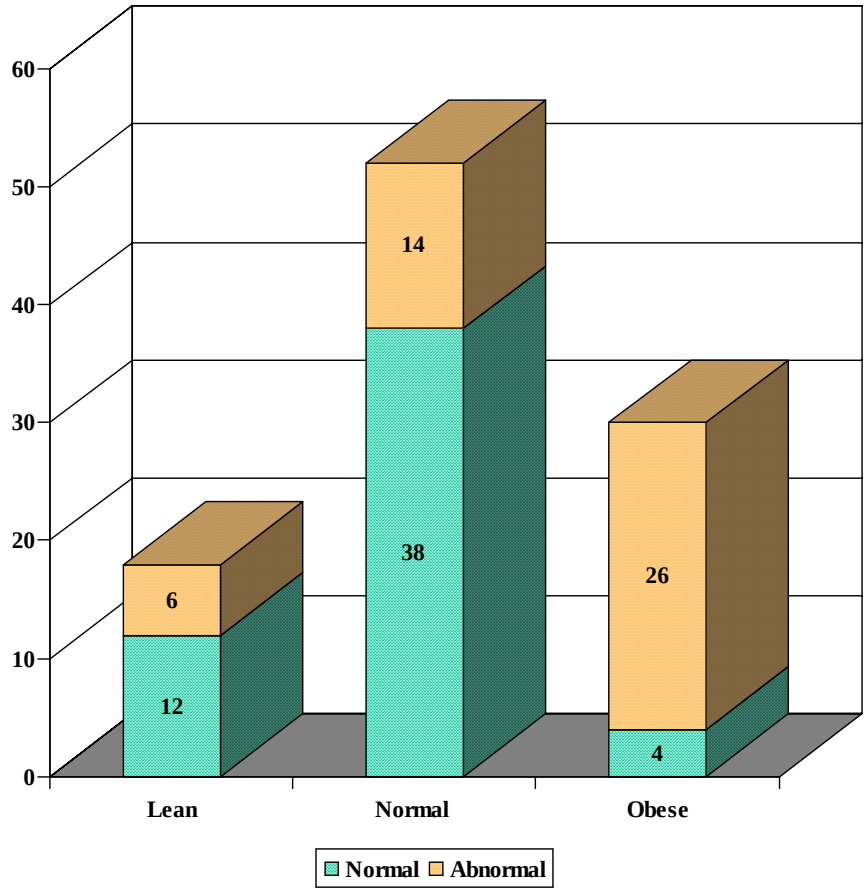
ECG

X ray	1. chest
(for selected patients)	2. Abdomen

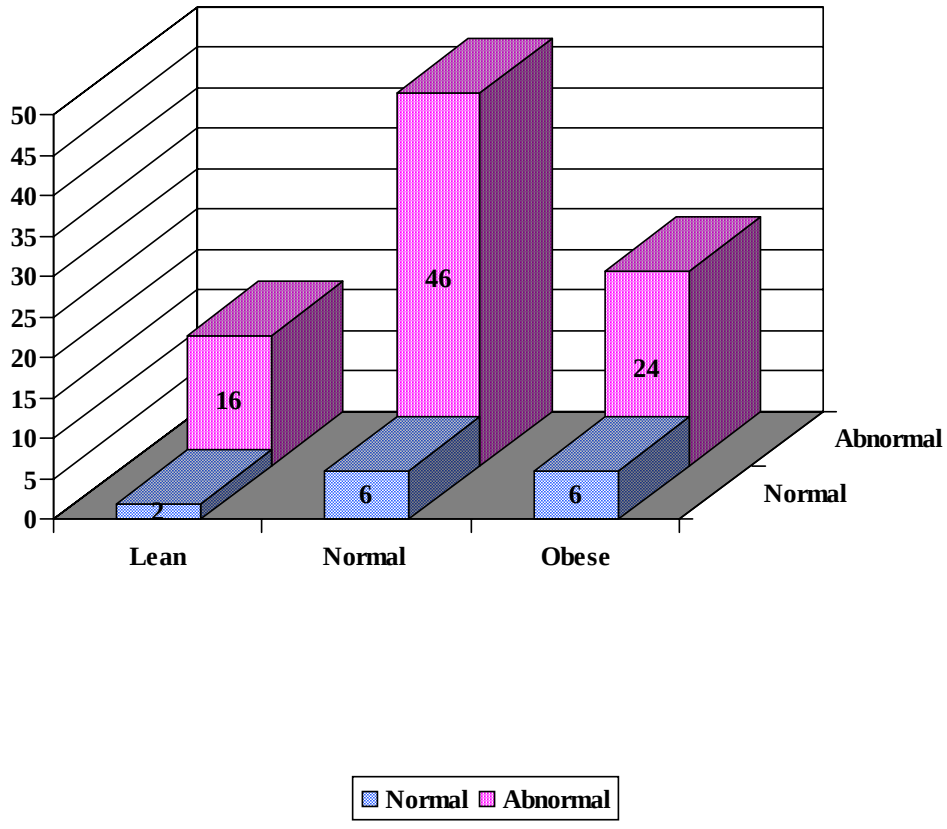
ASSESMENT

1 Type 2 DM	lean	
	Normal wt	
	Obese	
2 Family history	Present	Absent
3 Metabolic	Fasting Hyperglycemia	Yes/No
4 vascular	IHD	Yes/no
	PVD	Yes/no
	Cardiomyopathy	Yes/no
	Retinopathy	Yes/no
	Nephropathy	Yes/no
	Neuropathy	Yes/no
	Infections	Yes/no
	other associated disorders specify	Yes/no

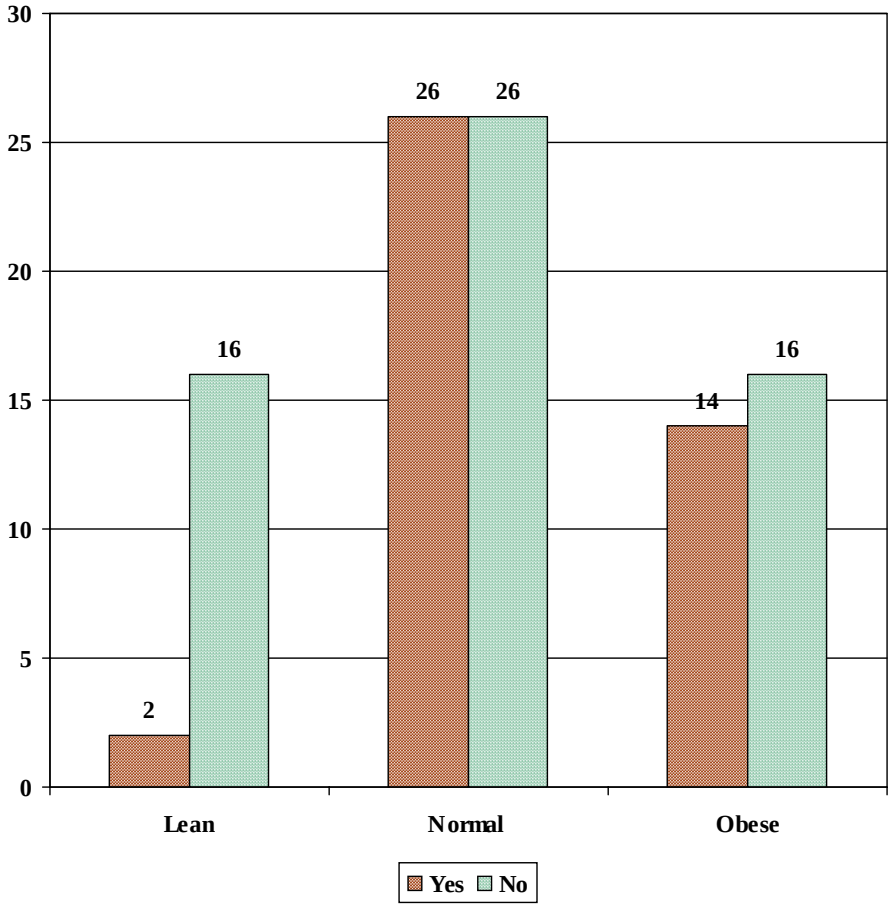
Waist Hip Ratio and BMI



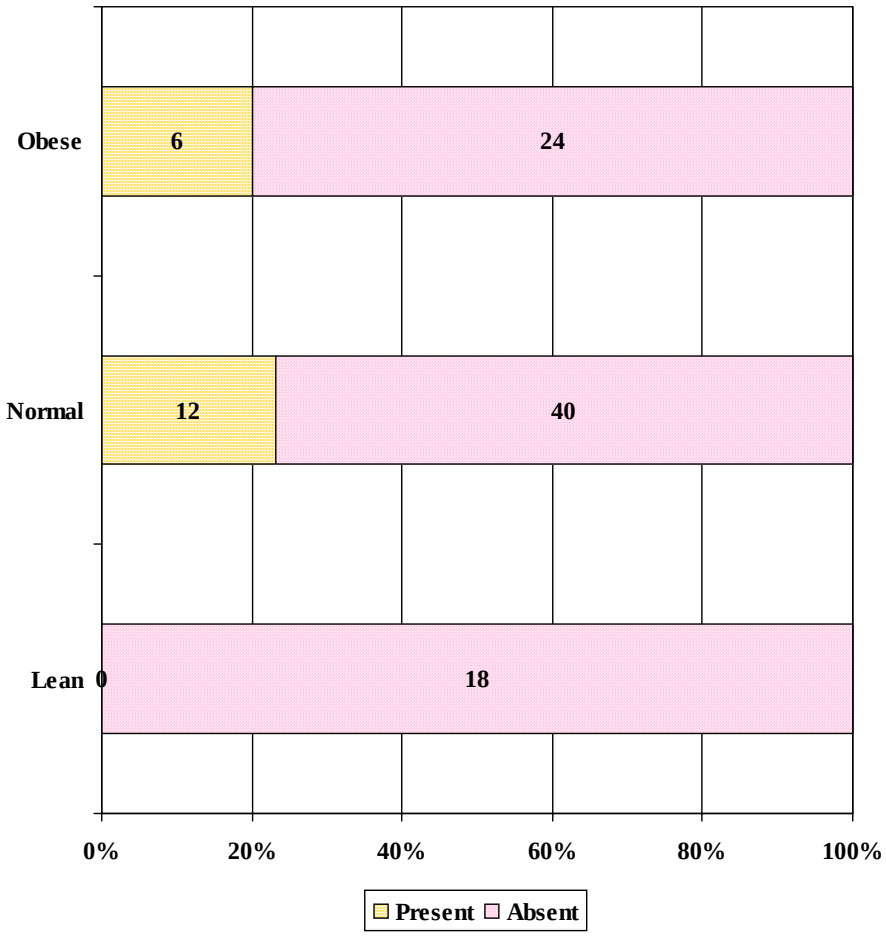
Fasting Blood sugar and BMI



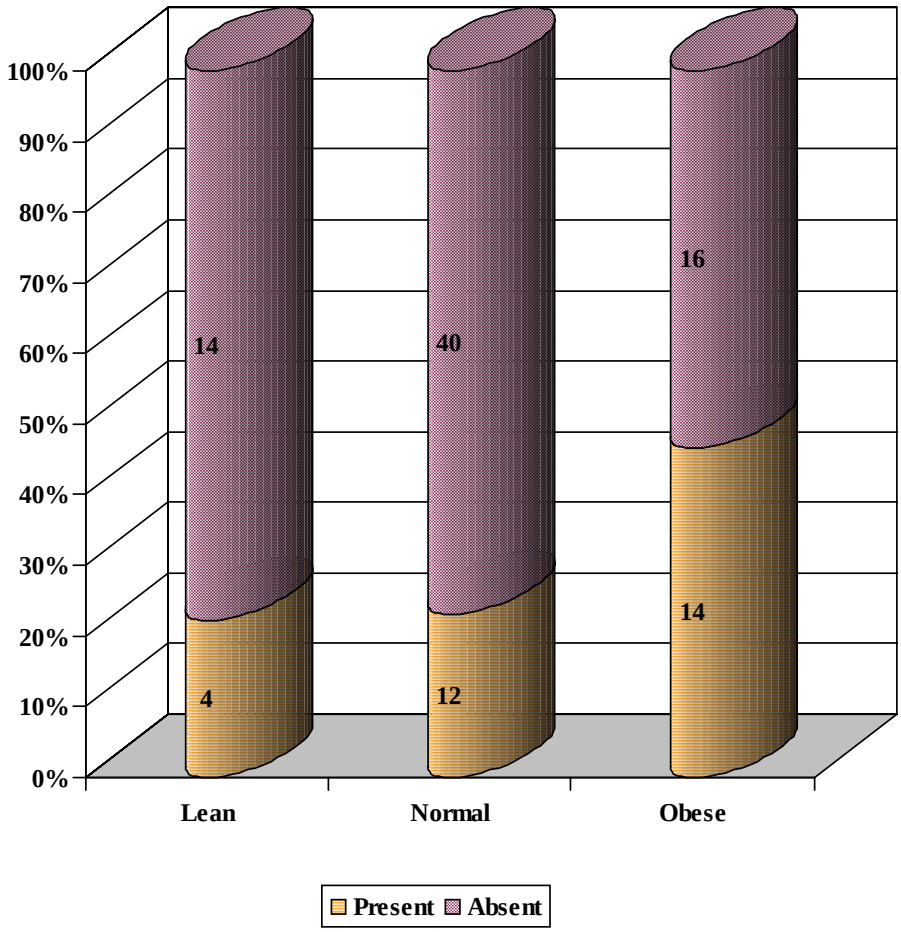
Family History and BMI



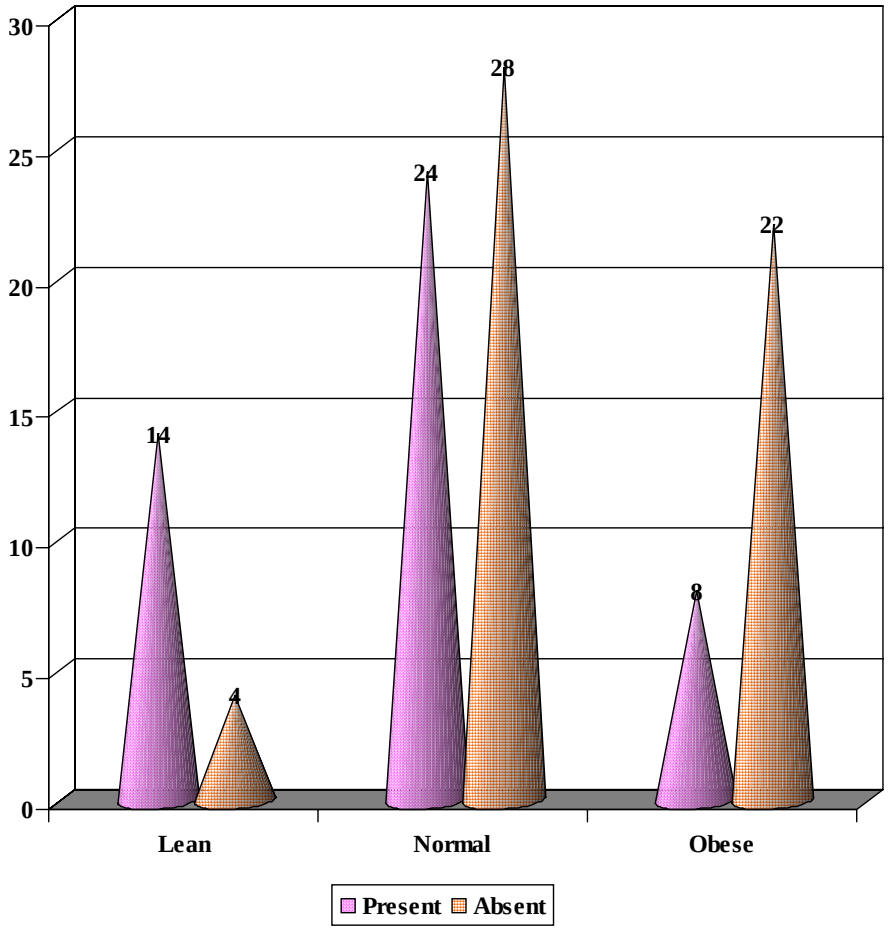
Cardiac and BMI



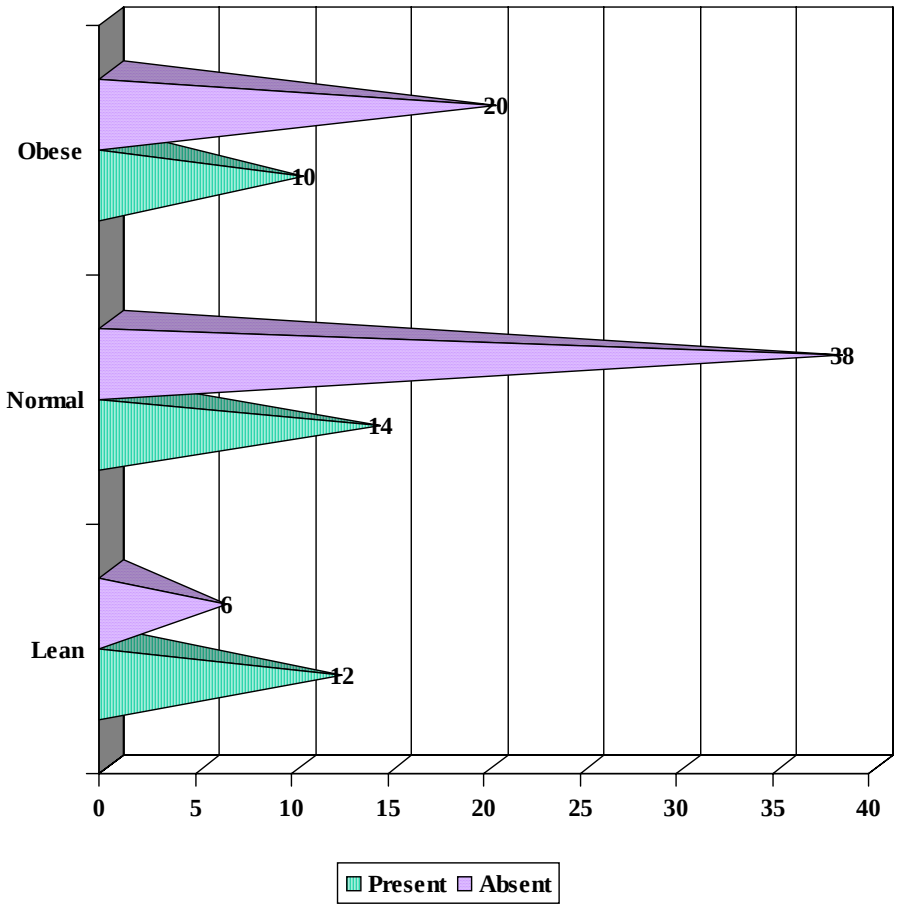
HT Incidence and BMI



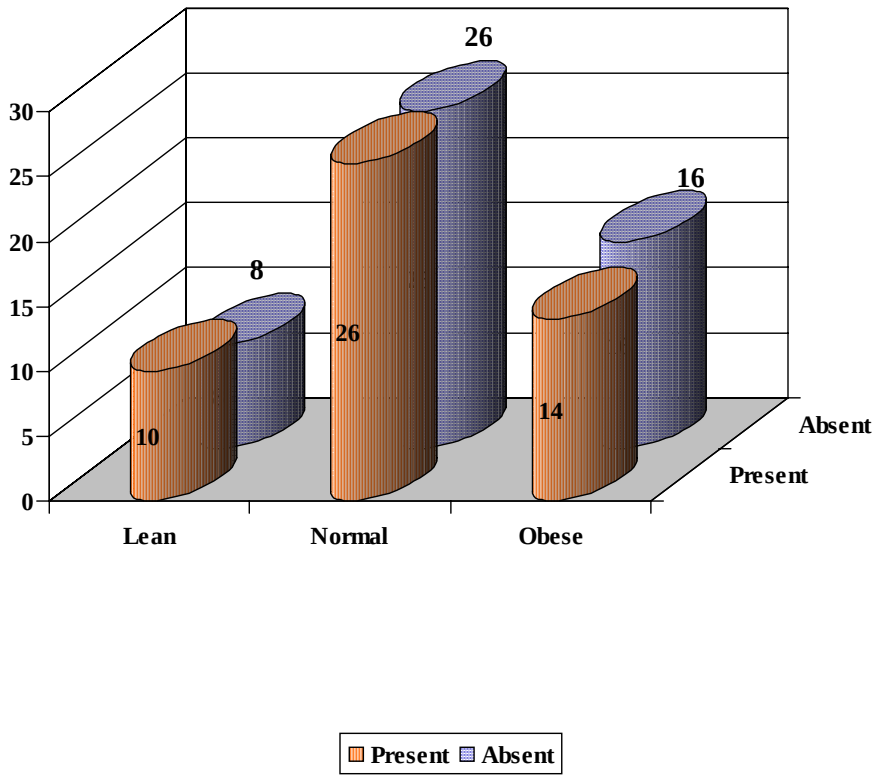
Neuropathy and BMI



Retinopathy and BMI



Renal and BMI



Infections and BMI